

Validated, Ultra Violet Spectroscopy method for the Dissolution study of Mycophenolate mofetil immediate release 500mg tablets

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Abstract:-

A simple, selective and precise dissolution method was developed and validated for the Mycophenolate mofetil immediate release tablets. The method employed dissolution medium 0.1N HCl (pH1.2) and volume 900ml with USP-II apparatus (Paddle). Detection was made by measuring the absorbance on UV at the λ_{\max} 250nm. The method show the linearity in the range of conc. 5 μ g/ml to 40 μ g/ml with $r^2=0.999$. The method is also validated as per International Conference of Harmonization guidelines. The method showed the specificity with standard deviation 0.00. The method is repeatable, selective and accurate for the dissolution study of Mycophenolate mofetil immediate release tablets.

Key words:-

Mycophenolate mofetil, immediate release tablets, dissolution medium, International Conference of Harmonization, Validation

Introduction:-

Mycophenolate mofetil is a white or almost white crystalline powder act as immunosuppressive drug. It is the ester moiety of Mycophenolic acid. As category specified the drug is used for the immunity suppression in organ transplant so it is required to prepare an immediate release formulation to produce rapid effect during organ transplant. There is no official method for the dissolution study of mycophenolate mofetil 500mg tablets [12]. As per BCS (Biopharmaceutic Classification System) the drug belongs to Class II i.e. having low solubility in water but high permeability, so its IVIVC (invivo-inviro correlation) accepted for this drug [17]. This method provides a simple IVIVC of mycophenolate mofetil tablet as per the requirements for the immediate release tablets. The objective of the present work was to develop

and validate an accurate, specific, precise and repeatable method for dissolution study of mycophenolate mofetil IR tablets as per ICH guidelines [14].

Materials & methods:-

Materials:

Pure Mycophenolate mofetil was obtained as gift sample from Biocon Ltd., India. Mycophenolate mofetil IR tablets were formulated at Faculty of Pharmacy, Jamia Hamdard, New Delhi. Hydrochloric acid purchased from Qualigens fine chemicals, Mumbai.

Equipments:

UV-Visible spectrophotometers used in the experiment were from Perkin Elmer, Lambda 35, USA and Shimadzu, UV-2450. The dissolution apparatus from Distek, Dissolution system 2100C and Electrolab, TDT-08L, USP were used in the development and validation.

Method development:

Various dissolution Medias were tested for the development of a suitable dissolution method for the dissolution study of Mycophenolate mofetil in IR tablets [16]. At last the following parameters were selected:

Medium: 0.1N HCl (pH1.2)
Volume: 900 mL
Apparatus: USP type-II (Paddle)
RPM: 50
Temperature: $37 \pm 0.5^\circ\text{C}$
Time: 30 min.

Calibration Curve of Mycophenolate mofetil:

A stock solution of Mycophenolate mofetil ($500\mu\text{g mL}^{-1}$) was prepared in 0.1N HCl (pH 1.2). Different volumes of stock solution diluted to get 5, 10, 20, 30 and 40 $\mu\text{g mL}^{-1}$ in 0.1N HCl (pH 1.2). A linear standard curve was obtained between Absorbance and Concentration ($\mu\text{g mL}^{-1}$) with $r^2=0.9998$.

Preparation of test solution:

A tablet dropped into each of the six dissolution vessels containing preheated dissolution media 0.1N HCl (pH 1.2). Withdraw 10 mL aliquot of the sample at 5, 10, 15 and 30 mins intervals. Diluted 2 mL of aliquot to 50ml with dissolution media and filtered through 0.45 μm nylon membrane filter.

Preparation of standard solution:

Accurately weighed and transferred about 55mg of Mycophenolate mofetil working standard into a 50ml volumetric flask. Added about 10 mL of dissolution media and sonicated to dissolve it. Made up the volume with dissolution media and mixed. Diluted 2 mL of this solution to 100mL with dissolution media and filtered through 0.45 μm nylon membrane filter.

Measure the absorbance of standard and sample at 250nm by using UV Spectrophotometer and dissolution media used as blank.

Method validation:**Specificity:**

Scanning and absorbance measurement carried out for the blank (diluent used in the method), placebo and test solution. There was no interference from the blank and placebo was observed. (Fig.-1 and Fig.-2)

Precision:

Precision was determined at three levels i.e. system precision, method precision and intermediate precision. The percent RSD in first case was 0.1 and 1.02 and 1.00 respectively in last two cases.

Linearity:

The concentrations of Mycophenolate mofetil from 10-30 $\mu\text{g mL}^{-1}$ were prepared from stock solution (100 $\mu\text{g mL}^{-1}$) and absorbance of measured at 250nm. The graph was plotted between concentration and absorbance for linearity.

Accuracy:

The placebo samples were spiked with 70, 100 and 130% of the standard Mycophenolate mofetil in triplicate. And recovery of the drug at different levels is determined in formulation.

Filtration Recovery:

The test solution is centrifuged in triplicate. Also the test solution as a control and triplicate sample was filtered through nylon filter paper 0.45 μm , using fresh filter every time.

Solution stability of the analytical solution:

The sample solution analyzed initially and at different time intervals at room temperature for around 24 hrs.

Result and Discussion:**Method Development:**

The dissolution method developed with dissolution media 0.1N HCl (pH1.2) [10] is an official dissolution media and about 100% release of the drug from tablets was observed in 30 mints. So it is a good method for dissolution studies for IR tablets at 37 °C with 50 rpm. (Table-1)

Calibration Curve:

The linear regression data for the calibration curve of Mycophenolate mofetil showed a good linear relationship over the concentration range 5-40 µg mL⁻¹ with respect to absorbance. (Table-2)

Method validation:**Specificity:**

The blank and placebo solution has not given any interference as in scanning (fig.-1 and fig.-2). Placebo samples also had not shown any interference in absorbance at λ_{\max} 250nm. (Table-3)

Precision:

The intermediate precision and method precision of the method were determined as it produced % RSD 1.00 and 1.02 respectively. (Table-4 and Table-5 respectively)

Linearity:

The linearity in the range of 10-30 $\mu\text{g mL}^{-1}$ was shown in Table-6 with $r^2=0.9999$, intercept=0.0032 and slope= 0.0220 respectively.

Accuracy:

Complied recovery data shown in Table-7 for accuracy study. These expressed overall % RSD of 1.23 in three levels which was the less than the acceptance level of 10% [14].

Filtration recovery:

The percent drug dissolved obtained in all three cases shown the percent correlation 98.99 with each other. This was in the limit of acceptance 97-103 [5]. (Table-8)

Solution stability:

In the solution stability studies the percent drug present in the sample for 24 hrs was determined and it showed maximum cumulative %RSD 2.71 which was less than 5% of acceptance criteria [5]. (Table-9)

Conclusion:

The developed dissolution method is precise, accurate and stability indicating. The results from the statistical analysis prove that the method is repeatable for the dissolution studies of Mycophenolate mofetil IR tablets.

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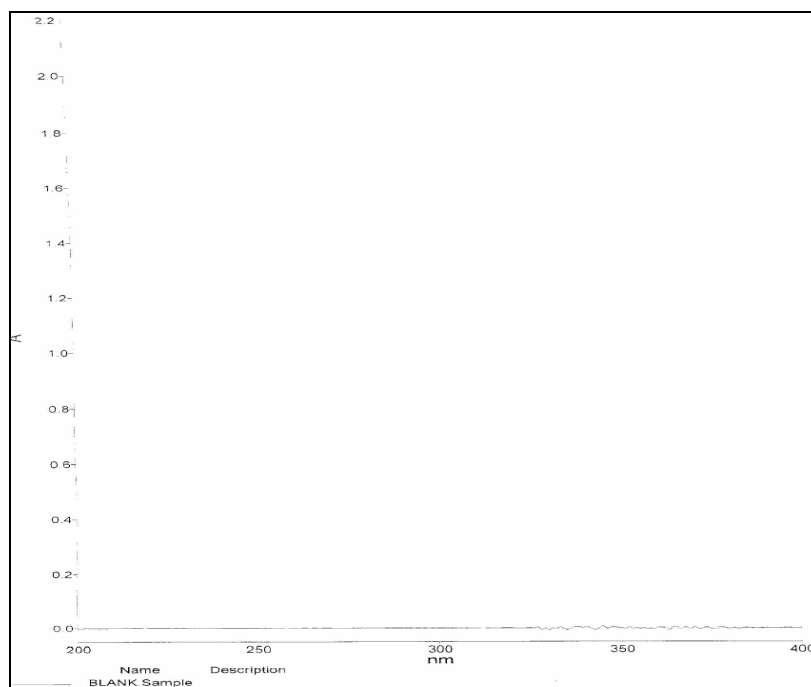


Fig. 1:- Scanning of blank at 250nm

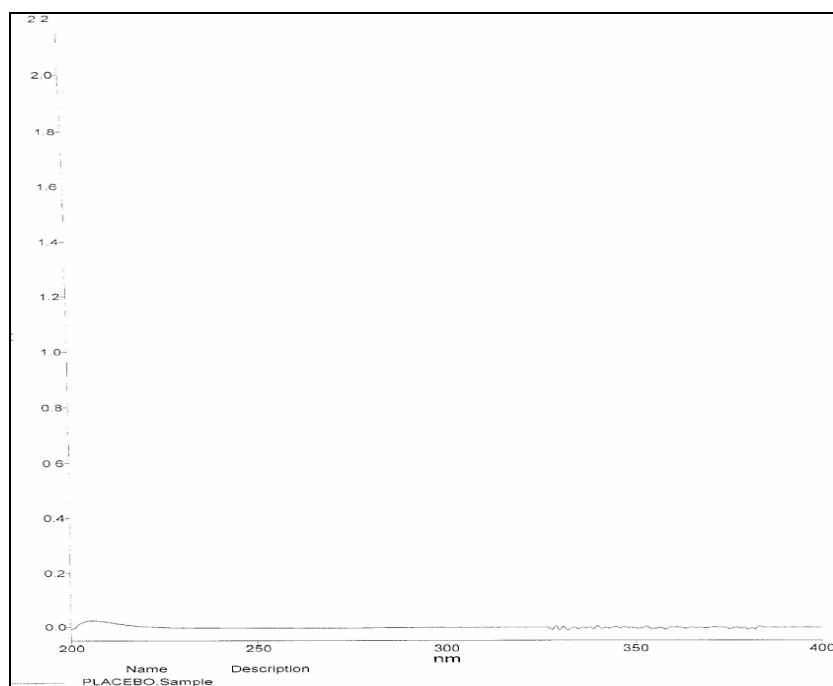


Fig. 2:- Scanning of Placebo at 250nm

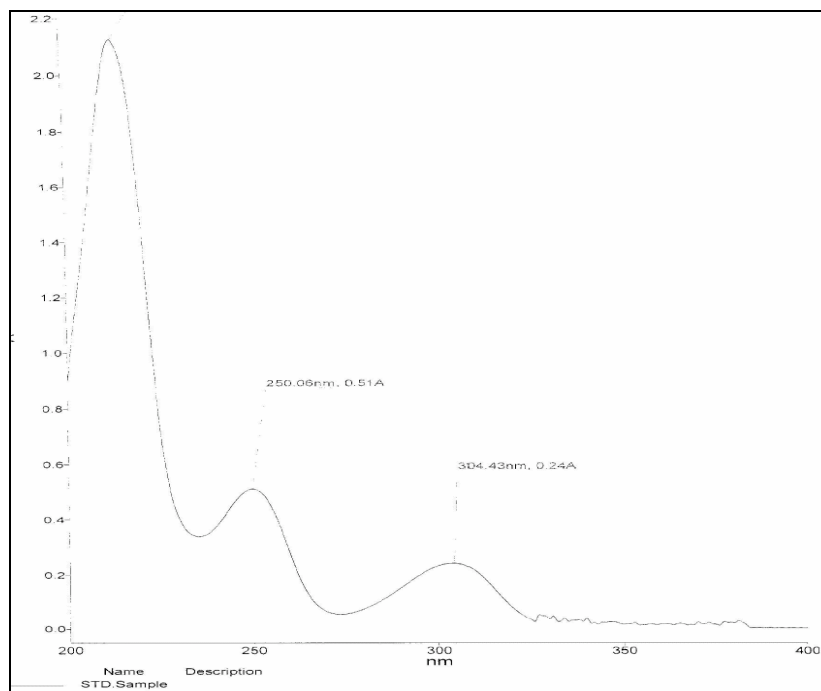


Fig. 3:- Scanning of Standard solution at 250nm

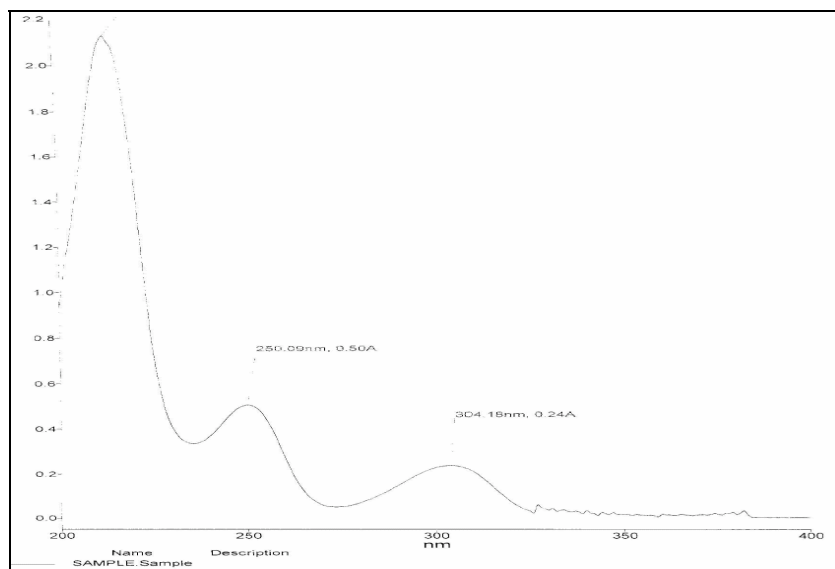


Fig. 4:- Scanning of Sample solution at 250nm